S/N 10/591,023

Remarks

Favorable reconsideration of this application is requested. Claim 1 is amended to limit the term "comprising" to "consisting of" and incorporates the subject matter of claim 7. Claim 15 has been amended similarly as claim 1 and also includes the subject matter of previously presented claim 18. Accordingly, claims 7 and 18 have been canceled and the dependency of claim 19 has been changed to depend upon claim 15. Withdrawn claims 14, 16, and 17 have been canceled without prejudice or disclaimer. No new matter has been added. Claims 1, 3, 4, 8, 15, and 19 remain pending.

The Examiner has rejected claims 1, 3, 4, 7, 8, 15, 18 and 19 under 35 U.S.C. § 103(a) as being unpatentable over Upadhyay et al. (US 6,251,383) in view of De Souza et al. (US 2002/0142055). Applicants respectfully traverse the rejection.

Claim 1 is directed to a method for the treatment of a renal disorder, specifically, chronic recurrent urinary tract infection, both complicated and uncomplicated in a mammal suffering therefrom. The method of claim 1 consists of administering standardized extract of *Tinospora cordifolia* as an immunoadjuvant in conjunction with conventional antibacterial therapy.

Claim 15 is directed to a method for the treatment of a renal disorder in a mammal suffering therefrom, consisting of administering to the mammal an amount effective for treating the renal disorder of a pharmaceutical composition consisting of a therapeutically effective amount of standardized extract of *Tinospora cordifolia* and a pharmaceutically acceptable carrier, in conjunction with conventional antibacterial therapy, wherein the renal disorder is a chronic recurrent urinary tract infection, both complicated and uncomplicated.

One of the necessary elements for establishing a *prima facie* case of obviousness is that the prior art reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F. 2d 488 (Fed. Cir. 1991). Applicants respectfully submit that such a *prima facie* case of obviousness has not been established.

Page 5 of the office action specifically refers to a portion (column 2 , lines 25 –40 under the heading "background of the invention") indicating that Upadhyay makes it clear that *Tinospora sp.* has been used in traditional Indian medicine for the treatment of urinary tract infection. The Examiner further adds that one having ordinary skill in the art would have been

motivated to use *Tinospora cordifolia* as claimed in the present invention since the plant was known for such a general use at the time the claimed invention was made.

With regard to the scope and content of Upadhyay et al., the reference is specifically directed to a method for ex vivo expansion of the number of hematopoietic cells for various clinical applications like transplantation of ex vivo expanded hematopoietic cells for restoration of immunocompetence, generation of activated and antigen sensitized immunocompetent cells for immunotherapy of cancer and infections, and ex vivo expansion of genetically transfected or transformed hematopoietic cells for gene therapy. In the Background of the Invention of Upadhyay et al., it is merely mentioned that plants of the Tinospora species have been widely used in traditional Indian medicine for treatment of skin infections, arthritis, fever, dysentery, urinary tract infections, and diabetes. However, there is no teaching or suggestion in Upadhyay et al. to use *Tinospora cordifolia* as an immunoadjuvant along with conventional antibacterial therapy in the treatment of recurrent urinary tract infections. Thus, Upadhyay et al. does not teach or suggest use of *Tinospora cordifolia* as an immunoadjuvant in conjunction with conventional antibacterial therapy.

Regarding De Souza et al., the Examiner states that the reference teaches standardization of an extract of *Tinospora cordifolia* by bioassay and use of such a standardized extract for administration to mammals. The Examiner further adds that De Souza et al. teaches that the extract is administered with a conventional therapy. On page 3 of the office action, the Examiner refers to Example 5, paragraphs 27-28, 31, 38-40, 44-50, 54, 60 and the claims of De Souza et al. for holding the claimed invention obvious. However, De Souza et al. teaches use of the standardized extract of *Tinospora cordifolia* as an adjuvant therapy in patients with osteomyelitis, cancer, diabetes and respiratory system disorders but no reference is made to urinary tract infections. In fact, example 5 in De Souza et al is specifically directed to use of the standardized extract as adjuvant therapy in patients with osteomyclitis. Moreover, the specification of De Souza et al. repeatedly makes specific reference to osteomyelitis, cancer, diabetes and respiratory system disorders as the diseases related to the immune system (paragraphs [0022], [0023], [0024], [0025], [0033], [0034], [0035], [0036] and [0037] and also the examples of US 2002/0142055). Thus, De Souza et al. provides no teaching or suggestion to one of skill in the art to use the standardized extract of *Tinospora cordifolia* as an adjuvant therapy in patients suffering from urinary tract infections. And since osteomyclitis and urinary

tract infections are not related disorders, a person of ordinary skill in the art also would not be motivated to look to De Souza et al. for use of the extract of *Tinospora cordifolia* as an immunoadjuvant specifically for the treatment of recurrent urinary tract infection.

On the other hand, the claims of the instant application as presented herein are specifically drawn to a method for the treatment of a mammal in need of treating chronic recurrent urinary tract infection. The Examiner has acknowledged at page 3 of the office action that Upadhyay does not explicitly teach that *Tinospora cordifolia* is used to treat urinary tract infections or that urinary tract infections are "chronic and recurrent" or that an antibacterial agent such as amoxicillin is used along with the extract. Therefore, in the absence of any teaching in the cited prior art references, a person having ordinary skill in the art would not be motivated to use a standardized extract of *Tinospora cordifolia* as an immunoadjuvant in conjunction with conventional antibacterial therapy for the treatment of a chronic recurrent urinary tract infection in a mammal who is in need of such treatment.

In view of the foregoing, taking into consideration the combined teachings of the Upadhyay et al. and De Souza et al. references, at best a person having ordinary skill in the art would be motivated to use the standardized extract of *Tinospora cordifolia* taught in De Souza et al in the culture medium of Upadhyay's method involving ex vivo expansion of the number of hematopoietic cells.

Consequently, Applicants respectfully submit that claims 1 and 15 and their respective dependent claims are patentable and not obvious over Upadhyay et al. and De Souza et al. taken alone or in combination.

The Examiner has rejected claims 1, 3, 4, 7, 8, 15, 18 and 19 under 35 U.S.C. § 103(a) as being unpatentable over Upadhyay et al. in view of De Souza et al. (both above), and further in view of Solanki (US 2003/0147896). The rejection is respectfully traversed for the reasons as provided below.

As described above, neither De Souza et al nor Upadhyay et al. teaches or suggests treatment of chronic recurrent urinary tract infection in a mammal in need of such treatment by using a standardised extract of *Tinospora cordifolia* or a composition containing such an extract as an adjuvant in conjunction with conventional antibacterial therapy. Solanki does not further the teachings of the prior art to render the claims obvious.

The Examiner cites Solanki on the basis that this reference allegedly teaches use of *Tinospora cordifolia* to treat a patient who has renal failure and that using the extract helped the kidneys in filtering excess protein and calcium. In the office action at page 7, a specific reference is made to paragraphs 3, 24 and 25 of Solanki.

In paragraph 3 of the specification, Solanki specifically indicates that the invention is related to a polyherbal composition which comprises a mixture of the following seven herbs: *Tinospora cordifolia, Chlorphyton boriviliapum, Curcuma longa, Asparagus racemosus, Hygrophila auriculata, Achyranthus aspera and Elephantopus scaber*, or a mixture of the active ingredients that have been extracted from those herbs or chemically synthesized. Moreover, in paragraph 5 of Solanki (2003/0147896), it is specifically stated that "it is an important feature of the product of the present invention that it contains a mixture of herbs, or extracts from herbs, rather than being based on a single herb. A synergistic effect has been noticed between the various ingredients. This synergistic activity is surprising and unexpected." Thus, Solanki expressly teaches against, and basically precludes, use of a single herb including that of *Tinospora cordifolia* among other herbs.

Solanki does not teach or suggest, and rather excludes from its scope, a composition containing *Tinospora cordifolia* alone. Also, the reference is exclusively directed to use of the polyherbal composition itself for the treatment of cancer or as an adjuvant to conventional modes of anticancer therapy, namely radiotherapy and/or chemotherapy.

Thus, in view of the fact that Solanki expressly teaches against use of a single herb such as *Tinospora cordifolia*, a person of ordinary skill in the art would not be motivated to use a standardized or even a non-standardized extract of *Tinospora cordifolia* alone, as an immunoadjuvant in conjunction with conventional therapy for the treatment of chronic recurrent urinary tract infection in mammal who is in need of such treatment. Rather, Solanki is merely concerned with the advantages of using polyherbal composition containing *Tinospora cordifolia* along with six other herbs, for the treatment of cancer or as an adjuvant therapy in the treatment of cancer, particularly myeloma, but not the use of a standardised or even a non-standardised extract of *Tinospora cordifolia* alone, as an adjuvant in conjunction with conventional antibacterial therapy for the treatment of chronic recurrent urinary tract infection in a mammal who is in need of such treatment.

Moreover, the Applicant wishes to point out that the proper treatment of recurrent urinary tract infections is critical considering the resistance to conventional antibiotics (see e.g. Clin Microbiol Infect. 2004 Nov;10 Suppl 4:1-9, attached herewith). Applicants respectfully submit that the presently claimed invention satisfies the long felt need of effective treatment for recurrent urinary tract infections.

Consequently, the claims, particularly independent claims 1 and 15 and the claims dependent therefrom, are not obvious over the cited references alone or in combination.

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C.§ 103 (a) are overcome. Accordingly, Applicants submit that the claims as currently presented are in allowable condition and a notice to that effect is earnestly requested.

Respectfully submitted,

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Date: November 30, 2009

By _____
Name: Douglas P. Mueller
Reg. No. 30,300
Customer No. 52835

Clin Microbiol Infect. 2004 Nov;10 Suppl 4:1-9.

The need for new antibiotics.

Antibiotic Resistance Monitoring & Reference Laboratory, Specialist & Reference Microbiology Division, Health Protection Agency, London, UK. david.livermore@hpa.org.uk

Politicians and public health officials have joined specialist professionals in recognising antibiotic resistance as a threat to modern medicine. Their response has centred on minimising unnecessary antibiotic prescribing, aiming to reduce selection pressure for resistance. Despite a few hopeful trends (e.g., declining penicillin resistance among pneumococci in the UK), established resistance is proving hard to displace; moreover, new resistances continue to emerge and to proliferate at new sites. There consequently remains a strong need for new antibiotics, particularly those directed against multiresistant Gram-negative bacteria in hospitals. Already some nonfermenters of the genera Acinetobacter and Pseudomonas are resistant to all good antibiotics and many Enterobacteriaceae are resistant to all except carbapenems. There is also a growing need for new agents against community-acquired pathogens, including the agents of tuberculosis, gonorrhoea and urinary tract infections. Unless antibacterial development is re-energised, there is a serious risk that a growing proportion of infections, especially in hospitals, will become effectively untreatable.

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Abstract from PubMed of citation "Clin Microbiol Infect. 2004"

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Item 1 of 1

1. Clin Microbiol Infect. 2004 Nov;10 Suppl 4:1-9.

The need for new antibiotics.

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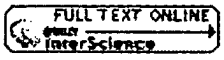

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- Review

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- Anti-Bacterial Agents/pharmacokinetics
- Anti-Bacterial Agents/therapeutic use*
- Bacterial Infections/drug therapy*
- Bacterial Infections/epidemiology
- Bacterial Infections/metabolism
- Bacterial Infections/microbiology
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- Drug Resistance, Multiple*
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- Public Health
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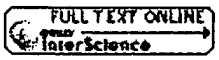

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[BMC Genomics. 2009]

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